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First-in-Human Evaluation of a Bioabsorbable Polymer–Coated Sirolimus-Eluting Stent

Imaging and Clinical Results of the DESSOLVE I Trial (DES With Sirolimus and a Bioabsorbable Polymer for the Treatment of Patients With De Novo Lesion in the Native Coronary Arteries)

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Objectives This first-in-human multicenter study sought to examine prospectively the safety and efficacy of a new, cobalt chromium thin-strut, coronary absorbable polymer–coated, sirolimus-eluting stent.

Background Bioabsorbable polymers on drug-eluting stents may lower the long-term risks of inflammation, delayed healing, and adverse events.

Methods We enrolled patients with symptomatic coronary artery disease with stable or unstable angina pectoris and >50% diameter stenosis, amenable to coverage with a ≤23-mm long stent in a vessel 2.5 to 3.5 mm in diameter. All patients received dual antiplatelet therapy after implantation. Patients, in groups of 10, underwent repeat angiography, intravascular ultrasound, and optical coherence tomography at 4, 6, or 8 months, and all patients were seen or contacted at 18 months of follow-up.

Results The median (range) in-stent late lumen loss (LLL) was 0.03 mm (−0.22 to 0.21 mm), 0.10 mm (−0.03 to 1.2 mm), and 0.08 mm (−0.01 to 0.28 mm), at 4, 6, and 8 months, respectively. At 18 months, the median in-stent LLL was 0.08 mm (−0.30 to 0.46 mm). On optical coherence tomography, the proportion of uncovered stent struts decreased from a median of 7.3% (range 0.4% to 46.3%) at 4 months to 0% (range: 0% to 3.4%) at 18 months. The percentage of neointimal volume obstruction by intravascular ultrasound increased from a median of 5.3% to 9.1% between 4 and 6 months and remained nearly unchanged thereafter through 18 months of follow-up. The only recorded major adverse cardiac event was a myocardial infarction.

Conclusions At 18 months of follow-up, this absorbable polymer–coated, cobalt chromium sirolimus-eluting stent was associated with a low and stable in-stent LLL, complete strut coverage, and no stent thrombosis. (First-In-Human Trial of the MiStent Drug-Eluting Stent [DES] in Coronary Artery Disease [DESSOLVE-I]; NCT01247428) (J Am Coll Cardiol Intv 2013;6:1026–34) © 2013 by the American College of Cardiology Foundation

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Compared with bare-metal stents (BMS), drug-eluting stents (DES) are associated with markedly lower restenosis rates after percutaneous coronary interventions (1–3). However, the polymer coating that elutes the antiproliferative drug has been linked to complications including delayed vessel healing, hypersensitivity reactions, neoatheroma, and restenosis, with the potential for repeat intervention, stent thrombosis (ST), acute myocardial infarction (MI), and sudden death (4–6). The potential link between the permanent polymer and late adverse events has prompted the development of biodegradable sources of drug delivery to a stented vessel. Several next-generation designs emerged recently, including DES with reservoirs containing the drug and a variety of biodegradable polymer coatings (7–10). Absorption of the polymer may lower the rates of ST, particularly beyond 1 year after stent implantation. In addition, stents with absorbable polymers (APs) may allow a shorter duration of dual antiplatelet therapy (DAPT) than currently recommended (11,12).

The MiStent Sirolimus Eluting Absorbable Polymer Coronary Stent System, or MiStent (Micell Technologies, Durham, North Carolina) sirolimus-eluting stent (SES), was developed using a cobalt-chromium stent with very thin, 64-μm struts coated with crystalline sirolimus in a fully AP (Fig. 1). Compared with existing DES, the unique combination of crystalline sirolimus and AP enables the deposition of drug into the surrounding tissue and its prolonged elution at a controlled rate, providing therapeutic tissue concentrations of sirolimus through 6 months post-implantation, without an initial burst of drug release. The coating is cleared from the stent in 45 to 60 days and absorbed into the tissue within 90 days, leaving an inert BMS, as confirmed during pre-clinical animal testing (13). This approach of drug delivery to the artery is aimed at achieving tissue coverage of the stent struts without excessive neointimal proliferation.

The primary objectives of the DESSOLVE (DES With Sirolimus and a Bioabsorbable Polymer for the Treatment of Patients With De Novo Lesion in the Native Coronary Arteries) study, the first-in-human study, were to provide a preliminary evaluation of the safety and efficacy of the MiStent APSES for percutaneous coronary intervention in the treatment of patients with symptomatic ischemic heart disease and to provide guidance for future randomized trial designs. We report here the angiographic, intravascular ultrasound (IVUS), and optical coherence tomography (OCT) imaging studies in patients at 4, 6, 8, and 18 months, as well as clinical outcomes through 18 months of follow-up. The planned total duration of follow-up is 5 years.

Patient Population and Methods

Enrollment. This prospective, nonrandomized, multicenter study was approved by the ethics committees of the participating medical centers, and all patients provided written informed consent to participate. They were enrolled between November 2010 and March 2011 at 5 centers in New Zealand, Belgium, and Australia (Online Appendix A). Patients presented stable or unstable angina pectoris or overt or silent myocardial ischemia and were candidates for treatment of a single de novo type A, B1, or B2 coronary lesion, according to the American College of Cardiology/American Heart Association classification (14). The study lesion was >50% in diameter in a reference vessel 2.5 to 3.5 mm in diameter and amenable to coverage with a ≤23-mm long stent. One additional lesion in a nontarget vessel could be treated before the study procedure; however, this was not considered part of the study. The inclusion/exclusion criteria are listed in Online Appendix B.

Schedule of follow-up visits and diagnostic investigations. Each patient underwent a baseline medical evaluation, and APSES implantation was performed using standard percutaneous procedures. After pre-dilation of the lesion, the stent was advanced to the lesion site and expanded using a semicompliant balloon. Baseline angiographic and IVUS data were collected according to the instructions of the respective core laboratories. After the procedure, creatine kinase–myocardial band fraction were measured 8 and 24 h after the index procedure.

Abbreviations and Acronyms

AP = absorbable polymer(s)
APSES = absorbable polymer-coated, sirolimus-eluting stent(s)
BMS = bare-metal stent(s)
CI = confidence interval
DAPT = dual antiplatelet therapy
DES = drug-eluting stent(s)
ISA = incomplete stent apposition
IVUS = intravascular ultrasound
LLL = late lumen loss
MACE = major adverse cardiac event(s)
MI = myocardial infarction
MLD = minimal lumen diameter
OCT = optical coherence tomography
QCA = quantitative coronary angiography
SES = sirolimus-eluting stent
ST = stent thrombosis
TLR = target lesion revascularization
TVR = target vessel revascularization

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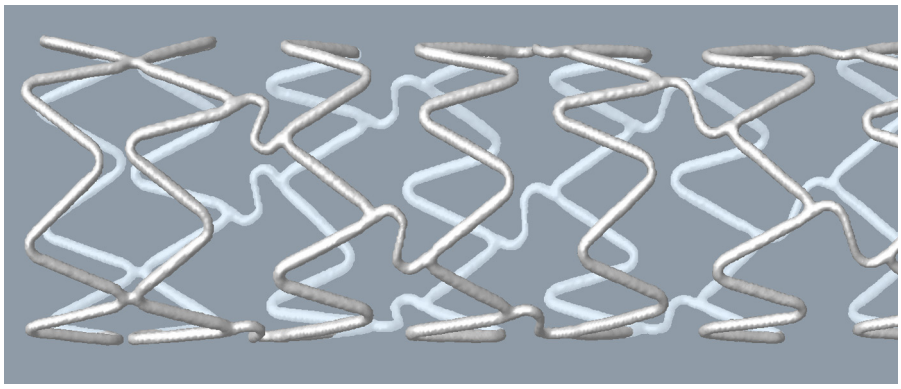

Figure 1. MiStent Sirolimus-Eluting Absorbable Polymer Stent

The design of the MiStent (Micell Technologies, Durham, North Carolina), constructed from cobalt chromium, is zigzag hoops that are largely in-phase with offset crowns linked by 3 S-shaped connectors per hoop. The connectors at both ends are straight and link crowns.

All patients received DAPT according to local practice, with a 12-month duration recommended.

All patients were contacted 30 days after the procedure. At 4 months, the first subgroup of 10 patients enrolled in the trial underwent repeat angiography, IVUS, and initial OCT of the target vessel (15,16). A second subgroup of 10 patients returned for the same diagnostic procedures at 6 months, and a third subgroup of 10 patients returned at 8 months. All patients had clinical assessments at 8 and 12 months and planned repeat angiography, IVUS, and OCT at 18 months (Fig. 1). All imaging studies were analyzed by independent core laboratories (Online Appendix A).

Study endpoints. PRIMARY. The primary endpoint of the study was angiographic in-stent late lumen loss (LLL), defined as the difference between the post-procedural minimal lumen diameter (MLD) in the stented segment and the MLD in the same segment at follow-up measured by the angiography core laboratory (Yale University, New Haven, Connecticut). The LLL was ascertained in the 3 subgroups of 10 patients at 4, 6, and 8 months and in 27 patients at 18 months of follow-up.

SECONDARY. The procedural secondary endpoints included device success, defined as a <50% final in-stent residual diameter stenosis by quantitative coronary angiography (QCA), using the MiStent SES device; lesion success, defined as a <50% final in-stent residual diameter stenosis by QCA using any percutaneous method; and procedural success, defined as a <50% final in-stent residual diameter stenosis by QCA using the assigned and any other device without cardiac death, MI, or repeat target lesion revascularization (TLR) before discharge from the hospital.

The invasive secondary endpoints, evaluated at 4, 6, 8, and 18 months of follow-up using QCA and the IVUS (Stanford University, Stanford, California) and OCT (Case Western, Cleveland, Ohio) core laboratories, included in-lesion LLL, percentage of diameter stenosis, MLD, and binary restenosis of the treated lesion. OCT was used to estimate the extent of strut coverage and volume of plaque and detect the presence of dissections, aneurysms, incomplete stent apposition (ISA), or thrombus. The heterogeneity of neointimal hyperplasia over time was tested by the measurement of a coefficient of variation. IVUS was used to assess the volume of hyperplasia and plaque, the presence and extent of ISA, and possible dissections and aneurysm formation and to measure the cross-sectional areas of stents and lumens.

The clinical secondary endpoints included major adverse cardiac events (MACE), defined as all deaths, Q- and non–Q-wave MI, and target vessel revascularization (TVR); rates of overall and target vessel Q-wave MI and non–Q-wave MI; rates of clinically driven TLR, TVR, and target vessel failure; and rates of ST, adjudicated according to the Academic Research Consortium definitions (17).

Device description. The stent platform is laser cut from a thin cobalt chromium alloy tube and electro-polished. The design of the stent is zigzag hoops with each hoop linked to the next by 3 connectors in the body of the stent. These links are "S" shaped and connect offset peaks (18). At each end the connectors are straight and short and link crowns. The stent is coated with antiproliferative crystalline sirolimus within a fully AP and mounted on a stent delivery system. The stent coating consists of poly lactide-co-glycolic acid, a biocompatible and biodegradable polymer used in many medical devices (19), combined with crystalline sirolimus. The drug and polymer coating deposited onto the stent is approximately 5 μm thick on the luminal side and 15 μm thick on the abluminal side. The coating process uses a proprietary method based on supercritical fluid technology

(13). The dose of sirolimus is 9 to 11 μg/mm and similar to that of the CYPHER SES (Cordis Corporation, Miami Lakes, Florida). Study stents were 15 or 23 mm in length and 2.5, 3.0, or 3.5 mm in diameter, on a rapid-exchange balloon delivery system.

Study monitoring and management. All investigational sites and data were monitored to ensure compliance with the protocol and verify that the data matched the source medical records. A clinical events committee adjudicated the study endpoints and pre-defined events that occurred throughout the study and a data and safety monitoring board reviewed all safety issues with regard to the ongoing study.

Statistical analyses. The analyses are limited to descriptive statistics and presented as count and percentage for categorical variables, mean ± SD and 95% confidence interval (CI), or median (range) for continuous variables. SAS version 9.1.3 SP2 (SAS Institute, Cary, North Carolina) was used for the analyses.

Results

Clinical and imaging compliance. Clinical information on 30 patients was collected through 18 months, corresponding to a 100% clinical compliance. Follow-up imaging studies were performed at 18 months in all but 3 patients; serious noncardiac diseases had developed in 2 patients and 1 patient declined to undergo the procedure. The 18-month

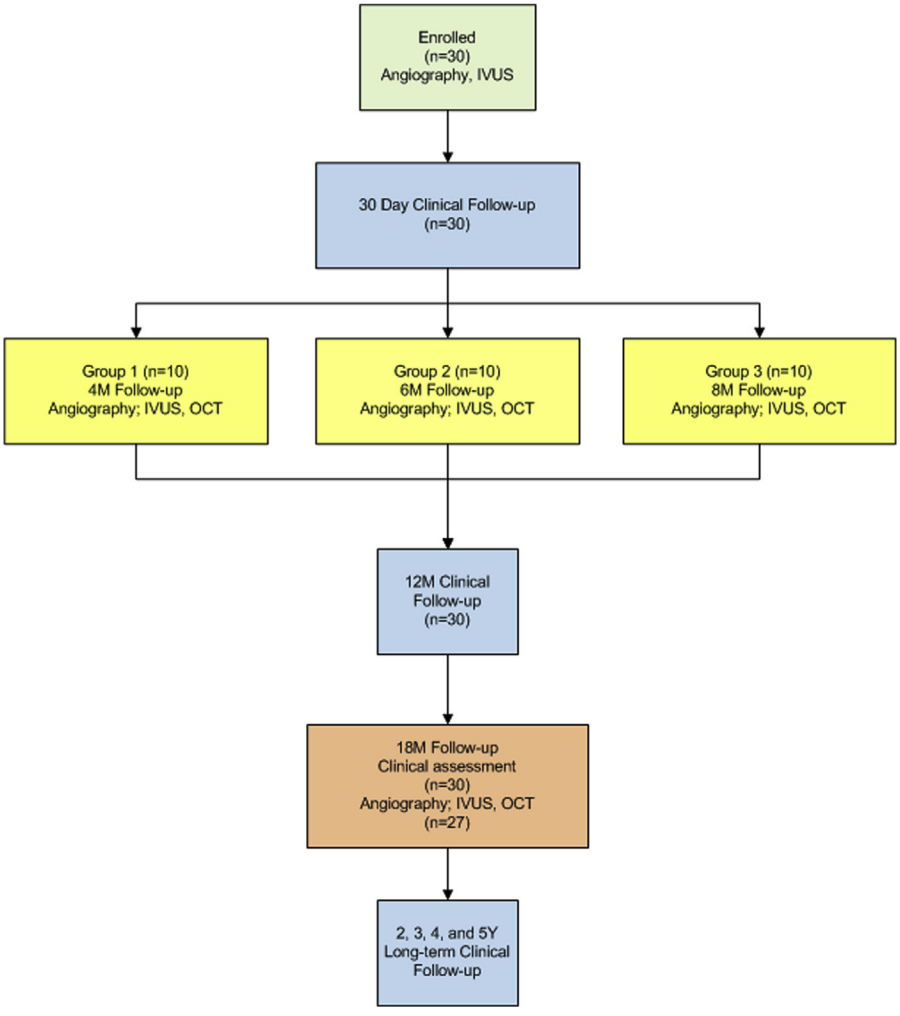

Figure 2. Sequence of the DESSOLVE I Study, From Initial Enrollment of 30 Patients to 18-Month Follow-up

Coronary angiography and intravascular ultrasound (IVUS) were performed at the time of study enrollment; angiography and IVUS were repeated, and optical coherence tomography (OCT) was performed, at 4, 6, or 8 months and at 18 months of follow-up. All patients also underwent clinical evaluations at 30 days and 12 and 18 months of follow-up, which has been planned to continue at yearly intervals up to 5 years. DESSOLVE = DES With Sirolimus and a Bioabsorbable Polymer for the Treatment of Patients With De Novo Lesion in the Native Coronary Arteries.

imaging analyses are, therefore, limited to 27 patients (Fig. 2).

Characteristics of the study sample. The mean ± SD age of the overall study sample was 62.6 ± 9.95 years, 22 (73%) were men, 26 (87%) were hypercholesterolemic, and 7 (23%) were diabetic. Other important baseline characteristics of the 30 patients are shown in Table 1. The baseline angiographic characteristics are shown in Table 2. The lesion length was 13.2 ± 3.8 mm and the mean MLD was 0.9 ± 0.2 mm. In two-thirds of patients, the target lesion was classified as B1 or B2, according to the American Heart Association classification.

Procedural outcomes. Each patient underwent treatment of a single target lesion. The APSES was implanted using a semicompliant balloon with a maximum stent deployment pressure of 13.9 ± 2.7 atm and post-dilation occurred in 76.7% of patients. The post-procedure in-stent MLD was 2.8 ± 0.3 mm (95% CI: 2.7 to 2.9 mm) and residual percentage of diameter stenosis was 2.3 ± 7.4% (95% CI: −0.5% to 5.0%). The lesion, device, and procedural successes were 100%, 96.7%, and 100%, respectively. In 1 patient, a first MiStent SES that had failed to cross a markedly calcified stenosis was removed, before the successful implantation of a second stent. Nonstudy stents were successfully implanted in 7 nontarget lesions before treatment of the target vessel.

Long-term angiographic results. The averaged QCA measurements made at 4, 6, and 8 months of follow-up in each subgroup of 10 patients and at 18 months in 27 patients are shown in Table 3. Compared with the immediate 2.8 ± 0.3-mm post-procedure in-stent MLD, the in-stent MLD (95% CI) in all 30 patients, up to 8 months, was 2.7 ± 0.4 mm (95% CI: 2.6 to 2.9 mm), corresponding to a mean ± SD in-stent LLL of 0.1 ± 0.2 mm (95% CI: 0.04 to 0.5 mm). In each subgroup of 10 patients, the median (range) in-stent LLL was 0.03 mm (−0.22 to 0.21 mm), 0.1 mm (−0.03 to 1.20 mm), and 0.08 mm (−0.01 to 0.28 mm) at 4, 6, and 8 months, respectively. The median (range) 4-, 6- and 8-month in-stent and in-lesion percentage of diameter stenosis was 5.4% (−12.8% to 46.6%) and 11.6% (−0.2% to 46.6%), respectively. The 18-month cumulative in-stent and in-lesion binary restenosis rates were both 0%.

IVUS studies. At the immediate post-procedural IVUS examinations, performed in 27 patients, edge dissection and ISA were observed in 1 (4%) and 4 (15%) patients, respectively. Of 4 post-procedural ISAs, 3 resolved by the follow-up visit and 1 persisted. Acquired ISAs were detected in 2 patients, resolved by 18 months of follow-up in 1 patient. No increase in vessel volume index >20% (positive remodeling) was observed.

An increase in neointimal obstruction was observed up to 8 months of follow-up, followed by no further progression up to 18 months, and the peristent plaque volume had returned to baseline level at 18 months. These IVUS observations were consistent with significant neointimal suppression and a favorable peristent arterial response at

Table 1. Baseline Characteristics of 30 Patients Enrolled in the DESSOLVE I Study

Age, yrs	62.6 (44–86)
Men	22 (73)
History of:	
Myocardial infarction	5 (17)
Percutaneous coronary intervention	12 (40)
On nontarget vessel	9 (30)
On target vessel	3 (10)
Coronary risk factors	
Hypercholesterolemia	26 (87)
Past or current smoking	23 (77)
Hypertension	23 (77)
Diabetes	7 (23)
Indications for index procedure	
Angina	
Stable	21 (70)
Unstable	6 (20)
Silent ischemia	3 (10)

Values are mean (range) or n (%) of observations.
DESSOLVE = DES With Sirolimus and a Bioabsorbable Polymer for the Treatment of Patients With De Novo Lesion in the Native Coronary Arteries.

Table 2. Baseline Angiographic Characteristics

Target vessel	
Right coronary artery	12 (40) (23–59)
Left anterior descending coronary artery	11 (37) (20–56)
Left circumflex coronary artery	7 (23) (10–42)
Reference vessel diameter, mm	2.9 ± 0.3 (2.7–3.0)
Lesion length, mm	
Mean	13.2 ± 3.8 (11.7–14.6)
<10	8 (27) (12–46)
10–19	21 (70) (51–85)
≥20	1 (3) (0.1–17)
Minimum luminal diameter, mm	0.9 ± 0.2 (0.8–1.0)
Percentage of diameter stenosis	69 ± 8 (66–72)
TIMI flow	
2	2 (7) (1–22)
3	28 (93) (78–99)
Complex characteristics	
≥45° bend	5 (17) (6–35)
Eccentric lesion	3 (10) (2–27)
Calcification	
Moderate	7 (23) (10–42)
Severe	1 (3) (0.1–17)
American Heart Association lesion class	
A	6 (20) (8–39)
B1	13 (43) (26–63)
B2	7 (23) (10–42)
C	4 (13) (4–31)

Values are n (%) of observations (95% CI) or mean ± SD (95% CI).
CI = confidence interval; TIMI = Thrombolysis In Myocardial Infarction.

Table 3. Results of Follow-up Quantitative Coronary Angiography at 4, 6, and 8 Months Each in 10 Patients and at 18 Months in 27 Patients

	Months			
	4 (n = 10)	6 (n = 10)	8 (n = 10)	18 (n = 27)
Reference vessel diameter, mm	2.8 (2.0 to 3.4)	2.9 (2.6 to 3.7)	2.9 (2.6 to 3.2)	2.9 (2.1 to 3.7)
Minimum luminal diameter, mm				
In-stent	2.7 (1.8 to 3.0)	2.9 (1.4 to 3.3)	2.8 (2.4 to 3.1)	2.7 (1.7 to 3.4)
In-lesion	2.5 (1.8 to 2.7)	2.5 (1.4 to 3.0)	2.6 (1.7 to 2.9)	2.5 (1.6 to 3.4)
Percentage of diameter stenosis				
In-stent	5.6 (−8.4 to 17.2)	3.1 (−12.8 to 46.6)	6.9 (−4.3 to 13.8)	6.1 (−11.4 to 17.0)
In-lesion	12.0 (1.2 to 27.0)	12.6 (−0.2 to 46.6)	10.5 (7.2 to 41.8)	16.2 (4.7 to 42.3)
Late loss, mm				
In-stent	0.03 (−0.22 to 0.21)	0.10 (−0.03 to 1.2)	0.08 (−0.01 to 0.28)	0.08 (−0.30 to 0.46)
In-lesion	−0.06 (−0.15 to 0.19)	0.02 (−0.21 to 1.19)	−0.02 (−0.17 to 0.59)	0.04 (−0.43 to 0.70)
Binary restenosis	0	0	0	0

Values are median (range).

18 months, without late in-stent neointimal "catch-up" phenomenon. The values for each subgroup of patients at 4, 6, and 8 months and in 25 analyzable patients at 18 months are shown in Figure 3.

Optical coherence tomography. The OCT measurements are summarized in Table 4. The proportion of uncovered stent struts decreased from a median of 7% (range 0.4% to 46%) at 4 months, to 3% (range 0% to 35%) at 6 months, 4% (range 0% to 8%) at 8 months, and 0% (range 0% to 3%) at 18 months. The median percentages of stent struts malapposition at 4, 6, 8, and 18 months were 0.4% (range 0% to 23%), 0.7% (range 0% to 19%), 0.3% (range 0% to 2%), and 0% (range 0% to 1%), respectively. The neointimal tissue volume increased from a median of 6 mm^3 (range 2 to 17 mm^3) to 15 mm^3 (range 5 to 33 mm^3) between 4 and 6 months of follow-up and remained numerically similar between 6 and 18 months of follow-up.

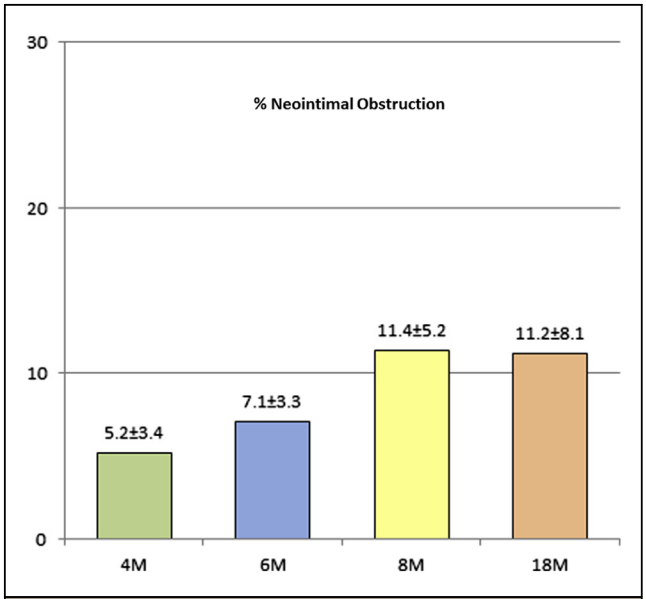

Figure 3. Percentage of Neointimal Obstruction on Serial Intravascular Ultrasound Examinations at 4 (n = 8), 6 (n = 5), and 8 (n = 7) Months of Follow-Up

Note the minimal increase in neointimal obstruction between the averaged 4-, 6-, and 8-month (n = 20) and the 18-month (n = 20) measurements.

Antithrombotic therapy. At the time of discharge from the hospital, all patients were on a DAPT regimen, including aspirin and either clopidogrel, ticlopidine, or prasugrel, and 73% continued on DAPT for 12 months. This decrease in DAPT duration was associated with no thrombotic event.

Clinical events up to 18 months of follow-up. No patient died or experienced TLR, TVR, or ST during the 18 months of this study. One patient had a non–Q-wave MI at 44 days after the index procedure as determined by increased levels of troponin after a diagnostic angiogram. The cumulative 18-month MACE rate was 3.3%.

Discussion

This first-in-human study was designed to examine the temporal patterns of tissue healing and the proof-of-concept for restoration to a BMS. We chose 4 months post stent deployment as the first assessment point because the polymer coating is completely absorbed at ~3 months. Repeated imaging at 6, 8, and 18 months allowed a detailed assessment of the tissue strut coverage, strut malapposition, positive remodeling, and other changes that have been associated with some of the durable polymer DES.

Our study confirmed, up to 18 months, the preliminary safety and efficacy of the cobalt chromium thin-strut MiStent SES, from which a poly lactide-co-glycolic acid

Table 4. Optical Coherence Tomography Analysis in Each Subgroup of 10 Patients and in 27 Patients Who Underwent Interventional Imaging at 18 Months

	Months			
	4 (n = 10)	6 (n = 9)	8 (n = 9)	18 (n = 27)
% of uncovered stent struts	7.3 (0.4–46.3)	2.9 (0–35)	3.8 (0–8.5)	0 (0–3.4)
% of malapposed stent struts	0.4 (0–22.7)	0.7 (0–18.9)	0.3 (0–1.6)	0 (0–1.3)
Stent volume, mm^3	105 (51–196)	146 (66–272)	136 (83–268)	132 (57–284)
Lumen volume, mm^3	103 (45–187)	131 (60–268)	134 (64–204)	114 (36–211)
Neointimal volume, mm^3	6.0 (2.3–17.5)	14.6 (4.8–33.0)	18.1 (8.2–64.0)	16.4 (6.4–73.2)
% net volume obstruction	7.0 (2.3–22.9)	10.0 (5.6–18.8)	13.3 (6.0–23.9)	16.4 (6.1–47.8)
Neointimal thickness (hyperplasia), μm	2.6 (0.6–24.6)	96.5 (39.3–143.6)	144.5 (74.8–236.2)	132.4 (68.1–343.2)

Values are median (range).

polymer coating is absorbed in 45 to 60 days. Crystalline sirolimus is delivered locally in sustained, therapeutic concentrations up to 6 months, without initial burst. The small angiographic in-stent LLL at each time point, along with the low neointimal volume obstruction on IVUS, indicates stent efficacy. Of particular interest, and in contrast to many other SESs, there was no evidence of late "catch-up"; the angiographic LLL, neointimal volume on IVUS, and neointimal thickness on OCT were all stable between the early and 18-month follow-up.

ST after 1 year post-implantation has been a major concern for first-generation DES, with randomized trials and real-world registry data suggesting an unremitting incidence of ~0.6% per year (6,20). Currently, ST is the most feared long-term complication of DES implantation (10,21,22), as it commonly leads to MI or death (23). ST has been correlated with incomplete endothelialization and underexpansion of the stent (24). In addition, the durable polymer coating of first-generation DES has been identified as a factor associated with ST, especially beyond 1 year (4,21–23). The second-generation DES, with thinner struts and thinner, more biocompatible polymers, are associated with a suppression of the neointimal response and a more rapid re-endothelialization (25). Randomized trials and large registries of second-generation DES in selected patient populations have generally confirmed their non-inferiority or superiority compared with first-generation DES (26–28). A recent meta-analysis of studies of current-generation DES found a lower rate of ST at 2 years after implantation of the second-generation fluropolymer-coated, everolimus-eluting stent than after the deployment of a BMS or other DES (29,30).

Although ST is less frequent in the first 1 to 2 years after DES implantation, later adverse events do remain a concern. The 5-year follow-up of the SIRTAX late randomized comparison of SESs versus paclitaxel-eluting stents with permanent polymer found a continuous increase in angiographic LLL, and a 2% to 3% annual increase in MACE rate beyond the first year (31). The Japanese Cypher registry of nearly 13,000 patients reported an ongoing 0.26% annual rate of ST and 2.2% rate of TLR, without a decrease over time (32). Late MACE, including TLR, occur after the implantation of other permanent polymer DES designs (33,34), although the incidence of restenosis is lower with newer than with older DES (31).

Multiple factors may contribute to the incidence of MACE late after stent implantation. Ongoing inflammation is present in arteries stented with permanent polymeric DES and may contribute to neoatheroma, late "catch-up," and ST (35). Neoatheroma occurs earlier and is more common after DES implantation, although it continues to occur with BMS (36,37). The incidence of late adverse events is likely to be lower after the absorption of the polymer, such as from the MiStent SES, than after the implantation of the DES coated with a permanent polymer, as there is less ongoing inflammation than with permanent polymers. In a meta-analysis of randomized trials, metal DES that release an antiproliferative drug from an absorbable polymer coating had lower rates of TLR and ST, out to 4 years, than metal stents that released a drug from a durable polymer (10). It was hypothesized that the inflammatory response, a major contributor to the processes that cause late adverse events, is attenuated after the absorption of the polymeric coating compared with a persistent polymer. Thus, biodegradable polymers have the potential to lower the rate of long-term adverse events attributed to durable polymers.

Although second-generation DES compared with first-generation DES have decreased the risk of ST, there is a need to develop devices that lower that risk further as well as the reliance on DAPT after percutaneous coronary interventions. Despite the design of better DES and more "biocompatible" materials in the past decade, a risk of inflammation persists with all permanent polymers. DES coated with bioabsorbable polymers remain effective, while eliminating the risks of ST and decreasing the need for prolonged DAPT.

The association between permanent polymers and adverse vascular reactions has been clearly demonstrated. The randomized LEADERS (Limus Eluted from A Durable versus ERodable Stent) trial studies showed that a biolimus-eluting stent coated with a biodegradable polymer had a lower risk of adverse cardiac events associated with very late ST through 5 years of follow-up, improving the long-term clinical outcomes compared with SESs coated with a durable polymer (38). However, 1 study, the SORT OUT (Scandinavian Organization for Randomized Trials with Clinical Outcome) V trial, suggests that at 1 year of follow-up, there may be no additional clinical benefit between a biodegradable polymer biolimus-eluting stent and a first-generation durable polymer SES (39). However, long-term follow-up is still pending. Whereas the new generation of DES might be coated with various types of bioabsorbable polymer, with different times to complete absorption, most likely will confer the same vascular and clinical benefits by eliminating the permanent polymer-driven mechanisms leading to ST (40).

Study limitations. This is a small, nonrandomized, hypothesis-generating, first-in-human study. The antiproliferative efficacy and, in particular, the safety of the stent require confirmation in a larger randomized trial, which has already commenced.

Conclusions

This first-in-human study of the MiStent SES in simple coronary artery lesions revealed a >95% median strut coverage on OCT performed at 6 and 8 months of follow-up and, up to 18 months after device implantation, a small and minimally progressive in-stent LLL and no stent-related MACE. These results suggest that the MiStent is at least as effective as the durable polymer-based SES, or newer generation bioabsorbable polymer and bioabsorbable stent platforms. The apparent stability of intimal hyperplasia and the absence of late "catch-up" phenomenon warrant further randomized trials of this stent in larger sample populations.

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Key Words: absorbable polymer ■ coronary artery disease ■ coronary stent(s) ■ percutaneous coronary intervention ■ sirolimus-eluting stent(s) ■ stent thrombosis.

APPENDIX

For supplemental material, please see the online version of this article.